Supreme Court, U.S.
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In The
Supreme Court of the United States
October Term, 1997

BINGMAN LABORATORIES, INC.,
Petitioner,

v.

UNITED STATES OF AMERICA,
Respondents.

Petition For A Writ Of Certiorari To The United States Court of Appeals For The Sixth Appellate District

PETITION FOR WRIT OF CERTIORARI
With Appendix

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158 pp

QUESTIONS PRESENTED FOR REVIEW

1. The Court of Appeals held that Claimant was marketing a "new animal drug" in violation of 21 U.S.C. §331(a) notwithstanding the fact that Petitioner had safely marketed the product to consumers for more than forty years. Did this decision constitute error?

2. The Court further held that the 1962 "grandfather clause" contained in the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 321(v), is inapplicable in this case.

3. The Food and Drug Administration (FDA) seized Petitioner's product without first providing Petitioner with a hearing regarding the seizure. Did the FDA deprive Petitioner of the basic due process protections afforded by the Fifth Amendment?

LIST OF PARTIES TO THE PROCEEDINGS IN THE COURT BELOW

Petitioner Bingman Laboratories, Inc., a corporation organized and existing under the laws of the State of Ohio, and Respondent, the United States of America were the parties to the proceedings in the United States Court of Appeals for the Sixth Circuit.

There are no parent or subsidiary companies of Bingman Laboratories, Inc.

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Case No.

IN THE
SUPREME COURT OF THE UNITED STATES
October Term, 1997

UNITED STATES OF AMERICA,

Respondent,

v.

UNDETERMINED QUANTITIES OF CLEAR PLASTIC BAGS OF AN ARTICLE OF DRUG FOR VETERINARY USE, *et al.*,

BINGMAN LABORATORIES, INC.,

Petitioner

Petition for a Writ of Certiorari from the United States Court of Appeals for the Sixth Circuit

PETITION FOR WRIT OF CERTIORARI

OPINIONS BELOW

The Opinion for the United States Court of Appeals for the Sixth Circuit is not reported, but is a part of the Appendix to this Petition. See Appendix A. The Judgment of the United States District Court for the Southern District of Ohio is not reported, but is likewise attached as Appendix B.

STATEMENT OF JURISDICTION

The Court of Appeals entered its judgment on May 4, 1998. Petitioner

invokes this Court's jurisdiction under 28 U.S.C. §1254(1).

STATUTORY, REGULATORY AND CONSTITUTIONAL PROVISIONS INVOLVED

Statutory Provisions

The following are banned by 21 U.S.C. §331:

> "(a) The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.

21 U.S.C. §321(v) defines the term "new animal drug" as follows:

> "...any drug intended for use for animals other than man, including any drug intended for

use in animal feed but not including such animal feed, (1) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof; except that such a drug not so recognized shall not be deemed to be a "new animal drug" if at any time prior to June 25, 1938, it was subject to the Food and Drug

Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions."

Constitutional Provisions

The Fifth Amendment to the United States Constitution provides, in part, that "no person *** shall *** deprived of life, liberty, or property, without due process of law."

STATEMENT OF THE CASE

I. Statement of Jurisdiction in Courts Below

On August 5, 1994, Respondent United States of America filed a Complaint in the United States District Court for the Southern District of Ohio, Eastern Division, against Petitioner Bingman Laboratories, Inc. ("Bingman") seeking seizure and condemnation of animal drugs manufactured and marketed by Bingman. The case is a civil *in rem* action for seizure and condemnation brought pursuant to 21 U.S.C. §334 of the Federal Food

Drug and Cosmetics Act. The District Court therefore had jurisdiction by virtue of this statute.

On March 31, 1997, the Honorable Joseph P. Kinneary, Sr., Judge of the United States District Court for the Southern District of Ohio, Eastern Division, rendered an Opinion and Order sustaining the government's motion for summary judgment. (Appendix B)

On April 23, 1997, Bingman filed a Notice of Appeal to United States Court of Appeals seeking reversal of the erroneous judgment of the District Court. The Sixth Circuit had jurisdiction by virtue of 28 U.S.C. §1291.

On May 4, 1998, the Court of Appeals affirmed the judgment of the District Court. This appeal followed.

II. Statement of Relevant Facts

Bingman has marketed an animal health product called "WRM-Rid Dog Wormer" ("WRM-Rid") since 1952. WRM-Rid is a drug used to kill parasites in dogs and cats. (Affidavit of William D. Semple, President and General Manager of Bingman Laboratories, Inc., ¶ 3, attached hereto as Appendix H.) Prior to placing WRM-Rid on the market, Bingman contacted Dr. J.H. Collins, Assistant Veterinary Medical Director of the FDA who outlined the requirements for labeling drug products. The WRM-Rid formulations and labels were revised in accordance with the FDA suggestions. After this initial revision, neither Dr. Moskey, Veterinary Medical Director, nor Dr. J.H. Collins took exception to the marketing of WRM-

Rid as presently formulated and labeled (Semple Affidavit, ¶ 3).

In 1955, "WRM-Rid" was reformulated to replace santonin with piperazine. Bingman reformulated its product because piperazine was newly approved and a much more effective ingredient (Semple Affidavit, ¶ 4). From 1955 through 1991, the FDA made numerous inspections of the Bingman plant; however, the FDA never once took exception to the labeling of WRM-Rid or commented on the safety and/or efficacy of WRM-Rid (Semple Affidavit, ¶ 4). Even in 1978 after the FDA promulgated a regulation requiring a prescription legend on all arecoline products (See, FEDERAL REGISTER, vol. 43, No. 50, Tuesday, March 14, 1978), the FDA never took action against WRM-Rid, even

though the FDA performed numerous inspections of Bingman Laboratories, collecting both drug and label samples.

From 1955 to the present, WRM-Rid has not undergone a single change in formulation, i.e., Bingman has never altered the percentage of active ingredients, the labeling claims, or any part of the manufacturing process (Semple Affidavit, ¶ 5). **WRM-Rid has been used for over 46 years to treat approximately 3,000,000 dogs and cats with only five complaints regarding toxicity** (Semple Affidavit, ¶ 5) Few drugs can boast of similar records.

On April 9, 1991, the FDA informed Bingman that it had determined that Bingman was manufacturing adulterated and misbranded drugs in violation of the

Food, Drug and Cosmetic Act notwithstanding the fact that the FDA had approved the labeling and sale of WRM-Rid since the late 1950's. Immediately Bingman initiated communications with the government in an effort to demonstrate that the product was safe, effective, and fully in compliance with the law.

These efforts proved unsuccessful. On September 12, 1994, the FDA infringed upon Bingman's legal rights by seizing an undetermined amount of WRM-Rid.

SUMMARY OF ARGUMENT

I.

WRM-Rid is not a "new" drug within the contemplation of the Act. In the proceedings below, Bingman substantiated this position by producing scientific data that WRM-Rid was safe in 1962. The

FDA had no evidence that the drug is not safe--nothing to justify its present effort to seize the instant goods.

II.

Contrary to the holding of the courts below, WRM-Rid is unquestionably grandfathered according to the plain language of 21 U.S.C. § 321(v). As such, it is not a "new drug" subject to new drug application and testing. Bingman has sold and safely marketed this product for more than forty six years. This is precisely the situation contemplated by Congress in enacted the 1962 "grandfather clause". But the Courts below erroneously limited the provision, and essentially rendered it meaningless.

III.

The FDA unconstitutionally seized the product because it has taken property of Bingman without a hearing. It is a well-settled principle of our Constitution that property may be seized without a hearing only if there is an eminent danger calling for immediate action. *North American Cold Storage v. Chicago*, 211 U.S. 306 (1908). The instant case clearly falls short of an eminent danger since (1) the FDA has permitted its sale for over forty years, (2) there is absolutely no proof of danger to human or animal life, and (3) the FDA could have afforded Bingman a hearing on the merits prior to the seizure. Moreover, the decisions of the courts below approved of a pattern of

regulatory overreaching far exceeding the scope permitted by the Constitution.

ARGUMENT

Introduction

The Federal Food, Drug and Cosmetic Act prohibits the introduction of any "new drug" into interstate commerce unless the FDA has approved the drug as "safe and effective." 21 U.S.C. §355. The statutory definition of "new drug," however, expressly excludes a drug that is generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, . . . [and if the drug has] been used to a material extent

or for a material time under such conditions. 21 U.S.C. §321(p).

As a baseline, the Act prohibits " the introduction . . . into interstate commerce of any . . . drug . . . that is adulterated." 21 U.S.C. §331 (a). An "adulterated" drug is a "new" drug that is not the subject of either an approved application with the FDA or an effective investigational exception. 21 U.S.C. §351(a)(5). Thus, in general, if a drug is a "new" drug, it must be the subject of an application with the FDA; if it is not, the Act deems it to be an "adulterated" drug that may not be placed in interstate commerce.

A drug is a "new" drug within the meaning of the Act if the drug is "not generally recognized, among experts

qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof. . ." 21 U.S.C. §321(v).

The language requiring evidence of the safety and "effectiveness" of a new drug was not part of the 1938 Act. "Effectiveness" was added by Congress at the time of the 1962 amendments to the Act. See Pub.L. 87-781, §102, 76 Stat. 781 (Oct. 10, 1962) A "grandfather clause" in the 1962 amendments specifically exempts from the "effectiveness" requirement some drugs that were on the market in the United

States prior to 1962. This clause, found at 21 U.S.C. §321(v), provides:

"In the case of any drug which, on the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective application under section 505 of that Act, the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day."

The 1962 grandfather clause, then, relieved manufacturers of pre-1962 drugs from having to demonstrate the

effectiveness of their drugs, so long as the drugs were generally recognized among experts as safe for certain uses in 1962 and no new conditions of use for the drug are suggested by the manufacturer. See *United States v. Alcon Laboratories*, 636 F.2d 876, 879 (1st Cir.), *cert.denied*, 451 U.S. 1017 (1981).

I

The drug in issue was not a "new" drug within the meaning of the Food, Drug and Cosmetic Act.

The Courts below held that WRM-Rid is a "new" drug within this definition, and concluded that is was therefore an "adulterated" drug. However, the statutory definition of "new drug," however, expressly excludes a drug that

is generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, . . . [and if the drug has] been used to a material extent or for a material time under such conditions. 21 U.S.C. §321(p).

Evidence of the status of WRM-Rid is in dispute. Bingman provided the District Court with evidence establishing that the drug was generally recognized among experts as safe and effective for the uses set forth in the label. Particularly, Bingman provided evidence proving that (1) WRM-Rid has not undergone a single change in formulation

since its introduction in 1955-- i.e., Bingman Lab's has never altered the percentage of active ingredients, the labeling claims, or any part of the manufacturing process; (2) at the time of its introduction, WRM-Rid was considered safe and effective in the scientific and veterinary community; and (3) WRM-Rid is currently intended for use under conditions prescribed in the 1962 labeling. See Semple Affidavit ¶¶ 3, 7, 8, 9, 10, 11, and 12.

In order to classify WRM-Rid as a "new drug," the FDA must establish either of two factors. First, the manufacturer must have implemented a labeling change after October 9, 1962, which suggests new conditions of use; or second, presentation of new evidence which

suggests WRM-Rid is unsafe or ineffective.

The FDA presented no evidence of any kind indicating that either of these two conditions exist. Bingman never changed the WRM-Rid label recommending or suggesting new conditions of use. There are no scientific evidence or reports indicating that WRM-Rid is unsafe.

The question of "general expert recognition" has troubled trial courts and appellate courts for some time. **As a result, this issue has consistently been held to be a factual question for the jury.** *United States v. An Article of Drug (Neo-Terramycin)*, 725 F.2d 976, 978 (5th Cir. 1984); *United States v. Quick-O-Ver*, 274 F.Supp 443 (D.Md. 1967).

These holdings are based upon a solid foundation: when the FDA seeks seizure and condemnation in a "new drug" action, the drug manufacturer has a right to have certain issues decided by a jury. The Act itself expressly provides for a trial by jury of "any issue of fact." 21 U.S.C. §334(b). Further, it is well settled that seizure actions are actions at law guaranteed a jury trial under the Seventh Amendment. See *C.J. Hendry Co. v. Moore*, 318 U.S. 133 (1943).

II.

Bingman's product was covered by the grandfather clause, 21 U.S.C. § 321(v).

The District Court compounded its error by further concluding that the "grandfather clause" contained in the Federal Food, Drug and Cosmetic Act, 21

U.S.C. § 321(v), is inapplicable in this case.

WRM-Rid unequivocally meets all five conditions of the 1962 clause. It was commercially used or sold in the United States prior to 1962 (Semple Affidavit, ¶ 3); it was not within the definition of a "new drug" in 1938 (Semple Affidavit, ¶ 12); it was not the subject of an effective new drug application as of October 10, 1962 (Semple Affidavit, ¶ 12); it was generally recognized as safe in 1962 (Semple Affidavit, ¶¶ 7, 8, 9, 10, and 11); finally, it is currently intended for use under conditions prescribed in the 1962 labeling (Semple Affidavit, ¶ 12).

WRM-Rid has not undergone a single change in its manufacturing process or

formulation since 1955 (Semple Affidavit, ¶ 5). Furthermore, the percentage of active ingredients, label claims, and recommended dosages have never been altered; therefore, WRM-Rid meets the labeling requirement.

Some courts focus on two of these factors in determining the applicability of the grandfather clause. Specifically, this body of law requires that one seeking Grandfather Clause protection must demonstrate: (1) general acceptance among experts in 1962; and (2) that the drug has not undergone any "new conditions of use." WRM-Rid, without exception, meets both criteria.

A. WRM-Rid Is Safe and Effective

In 1962, WRM-Rid was recognized by both the scientific community at large,

as well as the FDA itself, to be both safe and effective. Significantly, on November 30, 1967, the FDA issued its own Intra-Office Memorandum stating that Adams No-Mo Dog Worm Expeller, an arecoline based product like WRM-Rid, was both safe and effective.

Moreover, numerous standard pharmacological texts in existence prior and up to 1962 establish that arecoline hydrobromide and piperazine were generally recognized as safe and effective treatments for claims on the WRM-Rid label. See *Premo Pharmaceutical Laboratories, Inc v. United States*, 629 F. 2d 795, 803 (2d Cir. 1980); *Weinberger v. Bentex Pharmaceuticals, Inc.* 412 U.S. 645 (1973).

B. The Product Label Is Unchanged

FDA records, compiled during the Agency's myriad inspections of the Bingman plant, attest that the WRM-Rid product has not undergone a single labeling change or "new condition of use" since the product was first marketed in 1955.

III.

The FDA's unjustified seizure of Bingman's product constitutes a violation of the Fifth Amendment and a dangerous and unwarranted expansion of regulatory power.

In its haste to remove a harmless and beneficial product from the stream of commerce, the FDA acted in total derogation and disregard of the Fifth Amendment to the United States Constitution. The FDA simply did not see

fit to afford basic due process the Bingman before it unilaterally seized product.

In *United States v. James Daniel Good Real Property*, 114 S. Ct. 492 (1993), the Court addressed application of the Fifth Amendment to civil forfeiture of property. The general rule is that an individual should receive predeprivation notice and a hearing. *Good*, 114 S. Ct. at 500- 01. "The purpose of this requirement is not only to ensure abstract fair play to the individual. Its purpose, more particularly, is to protect his use and possession of property from arbitrary encroachment - - to minimize substantively unfair or mistaken deprivations of property . . . ." *Fuentes*

v. Shevin, 407 U.S. 67, 80- 81 (1972), quoted in *Good*, 114 S. Ct. at 501.

Civil forfeiture is currently in vogue in regulatory circles. But the cavalier use of forfeiture comes at a high price for individuals and small businesses. Where forfeiture is "[u]nfairly wielded it can place commercial enterprises at a terrible disadvantage." *United States v. All Funds on Deposit in Any Accounts, Merrill Lynch*, 801 F. Supp. 984, 989 (E.D.N.Y. 1992) aff'd, 6 F.3d 37 (2d Cir. 1993).

In *Good*, *supra*, the Court concluded that determining whether a particular seizure of property justifies an exception to the general rule providing notice and a hearing requires "an

examination of the competing interests at stake." See, also, *Mathews v. Eldridge*, 424 U.S. 319, 335 (1976). In *Good*, the Court applied the *Mathews* test to the forfeiture at issue, and found that the private interest affected - - the property interest in a person's home - - "weigh heavily in the Mathews balance." *Good*, 114 S. Ct. at 501.

FDA's seizure of Bingman's product affected a vital interest: the sole product of the corporation. No exigent circumstances justified this seizure without notice and hearing as guaranteed by the Fifth Amendment. Significantly, the *Good* Court placed the burden on the government to demonstrate that there were exigent circumstances that would justify

not providing the owner with notice and a hearing. *Id.* at 505.

This is a burden the FDA simply cannot meet. The seizure was contrary to the bedrock due process protections of the Fifth Amendment--a fact little noted by the Courts below.

In *Maryland v. Wirtz*, 392 U.S. 183 (1968), this Court wisely stated that "the power to regulate commerce, though broad indeed, has limits" that "[t]he Court has ample power" to enforce. *Id.*, at 196, overruled on other grounds, *National League of Cities v. Usery*, 426 U.S. 833 (1976), overruled by *Garcia v. San Antonio Metropolitan Transit Authority*, 469 U.S. 528 (1985). This Court should enforce these limits here.

Bingman's product was safe, and beneficial to consumers. The FDA's conduct was justified only by a hyper-technical reading of the law that ignored the history and clinical evidence.

To permit an agency to seize property based only on its own flawed legal analysis is an alarming precedent, for it leaves all citizens at risk of limitless regulatory overreaching. The basic protections embodied in the Bill of Rights were designed to prevent such governmental misconduct. The Court should grant certiorari to address this Constitutional issue.

CONCLUSION

The regulatory procedure set forth by the Federal Food, Drug and Cosmetic Act and accompanying regulations presents

a series of complex interrelated legal and factual issues.

This case presents the Court with a rare opportunity to clarify the confusing if not contradictory law interpreting this legislation. Moreover, it would permit the Court to set guidelines to prevent governmental agencies from reaching beyond the scope of their legislative mandate in disregard of the basic due process rights of citizens.

For these reasons, Petitioner Bingman Laboratories, Inc. urges this Court to grant certiorari in this case.

Respectfully submitted,

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APPENDIX A

UNITED STATES COURT OF APPEALS
FOR THE SIXTH CIRCUIT

OPINION

Sixth Circuit Case №. 97-3467
Filed May 4, 1998

Pages A-1 thru A-3

NOT FOR PUBLICATION

No. 97-3467

UNITED STATES COURT OF APPEALS
FOR THE SIXTH CIRCUIT

UNITED STATES OF AMERICA,
Plaintiff-Appellee,

v.

UNDETERMINED QUANTITIES OF CLEAR PLASTIC BAGS OF AN ARTICLE OF DRUG FOR VETERINARY USE, each bag contained a smaller clear plastic bag, paper label, and accompanying package insert, labeled in part (label) "*** WRM RID***Dog Wormer*** net weight 1 ounce Bingman Laboratories Sarahsville, Ohio***" (package insert) "***WRM RID Dog Wormer also for Cats***Bingman's*** Treatment *** Toxicity *** IMPORTANT *** Bingman Laboratories Sarahsville, Ohio ***" and all other quantities of the above article of drug for veterinary use in any size or type of container, and accompanying labeling, located on the premises of Bingman Laboratories, Inc., Mill Street, Sarahsville, Ohio,
Defendant,

ON APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE SOUTHERN DISTRICT OF OHIO

BINGMAN LABORATORIES, INC.,
Claimant-Appellant.

_____/

BEFORE: SUHRHEINRICH, SILER, and GILMAN, Circuit Judges.

PER CURIAM. In this in rem action under the Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C.A. §§ 301 -395 (West 1972 and Supp. 1998), Plaintiff United States of America is seeking to condemn Claimant Bingman Laboratories, Inc.'s veterinary drug, WRM-RID Dog Wormer ("WRM-RID"). The district court granted summary judgment to the United States. We **AFFIRM**.

The FDCA prohibits "[t]he introduction. . . into interstate commerce of any. . . drug . . . that is adulterated." *Id.* § 331(a). An "adulterated" drug, in turn, is a "new" drug that is not the subject of either an approved application with the Food and Drug Administration ("FDA") or an effective investigational exception. *Id.* §§ 351(a)(5), 360b(a)(1). A drug is "new' for purposes of the FDCA if it is not "generally recognized. . . as safe and effective" for use as recommended in its labeling. *Id.* § 321(p)(1). At the outset, the district court noted that WRM-RID was neither the subject of an approved new animal drug application or an effective investigational exception, either of which would permit its current sale to the public. The district court found that Bingman did not identify any substantial evidence, i.e., scientific clinical studies, that WRM-RID, as a combination drug, is generally recognized as safe and effective. In addition, the court held that Bingman did not establish that FDCA's grandfather clause applied to WRM-RID because Bingman did not show by substantial evidence that WRM-RID, as a combination drug,

was generally recognized as safe in 1962. *See* 21 U.S.C.A. § 321(v) note (West Supp. 1998) and 21 U.S.C.A. § 360b note (West 1972).[1] The court concluded that WRM-RID was a "new" drug and was, therefore, adulterated.

On appeal, Bingman argues that WRM-RID is not a new drug because it has been marketed for 43 years with no problems and, alternatively, that WRM-RID qualifies under the statute's grandfather clause. We disagree. After studying the record and the briefs of the parties, as well as the relevant law, we are satisfied that the district court correctly decided that WRM-RID was technically a "new" drug, the grandfather clause did not apply, and WRM-RID was not the subject of either an approved new animal drug application or an effective investigational exception that would permit its sale. Accordingly, we **AFFIRM** the judgment of the district court for the reasons stated in its opinion filed March 31, 1997.

---

[1]The grandfather clause exempts from the effectiveness requirement certain drugs on the market before 1962.

APPENDIX B

UNITED STATES COURT OF APPEALS
FOR THE SOUTHERN DISTRICT OF OHIO
EASTERN DIVISION

OPINION AND ORDER

Sixth Circuit Case №. 97-3467
Filed March 31, 1997

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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF OHIO
EASTERN DIVISION

UNITED STATES OF AMERICA,
Plaintiff,

V. Case No. C-2-94-0725

Undetermined Quantities of Clear Plastic bags of an Article of Drug for Veterinary Use . . . WRM-RID Dog Wormer . . .
Defendant.

OPINION AND ORDER

This matter is before the Court on the Plaintiff's motion for summary judgment. This civil in rem action was brought by the government under the Food, Drug and Cosmetic Act (the "Act") to request that this Court enter an order of condemnation and destruction against a seized article. The Court **GRANTS** the government's motion.

I. Facts

Bingman Laboratories, Inc. ("Bingman") has manufactured and marketed "WRM-RID Dog Wormer" ("WRM-RID") since 1952. WRM-RID is an animal drug promoted as a treatment for worms in dogs and cats. The

formula for WRM-RID has remained the same since 1955. The drug has two active ingredients:
piperazine phosphate and arecoline hydrobromide.

Prior to marketing WRM-RID, Bingman contacted the Food and Drug Administration ("FDA") to determine the requirements for marketing drug products. Bingman followed the agency's suggestions. Between 1955 and 1991, the FDA inspected Bingman's plant and took no exception to Bingman's marketing of WRM-RID.

On April 9, 1991, however, the FDA informed Bingman that WRM-RID was adulterated and misbranded in violation of the Food, Drug and Cosmetic Act. Bingman and the FDA engaged in a dialogue regarding the alleged violation. Nevertheless, the FDA filed a complaint alleging that WRM-RID is an "adulterated," "unsafe" "new animal drug" under the Act. Therefore, according to the FDA, WRM-RID is subject to forfeiture and condemnation under the Act. The FDA requests a warrant in rem directing the U.S. Marshall to retain and hold an undetermined amount of WRM-RID and to notify any interested individuals. The FDA also requests an order of forfeiture and condemnation of the seized WRM-RID.

On August 4, 1994, a warrant was issued and, on September 12, 1994, an undetermined amount of WRM—RID was seized. The government gave notice to all interested parties including Bingman. The FDA now seeks

summary judgment on its request for an order of forfeiture and condemnation.

Bingman opposes the FDA's motion on several grounds. First, Bingman suggests that it is inappropriate to establish the status of a drug on summary judgment. Second, Bingman argues that WRM-RID is grandfathered out of the Act's requirements. Third, Bingman argues that the FDA has failed to produce any evidence that WRM-RID is not safe and effective and therefore WRM-RID is not a "new" drug subject to forfeiture and condemnation. Fourth, Bingman asserts that WRM-RID was not in interstate commerce and so does not satisfy a jurisdictional prerequisite of the Act. Fifth, Bingman claims that the FDA'S seizure of WRM-RID violated Bingman's constitutional right to due process. Finally, Bingman suggests that the FDA's failure to prosecute Bingman for marketing WRM-RID in the past bars the current action.

II. SUMMARY JUDGMENT

A. Standard

Rule 56(c) of the Federal Rules of Civil Procedure provides as follows:

> (summary judgment] . . . shall be rendered forthwith if the pleadings, depositions, answers to interrogatories and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any

material fact and that the moving party is entitled to judgment as a matter of law.

Summary judgment is appropriate where, based on the documentary evidence, there is no genuine issue of material fact to be tried. Lashlee v. Sumner, 570 F.2d 107, 111 (6th Cir. 1978). The party moving for summary judgment bears the burden of establishing the absence of a genuine issue of material fact. Adickes v. S.H Kress, 398 U.S. 144, 157 (1970). In considering whether to grant a motion for summary judgment, a court must believe all of the non-moving party's evidence and draw all reasonable inferences from the evidence in her favor. Russo v. City of Cincinnati, 953 F.2d 1036, 1042 (6th Cir. 1992).

B. Appropriateness or Summary Judgment

Bingman asserts that "[s]ummary judgment motions by the FDA to establish a disputed product status are generally disfavored by the courts." (Doc. #9 at p. 4 (citing United States v. Article of Food Consisting of 345—50 Pound Bags, 622 F.2d 768 (5th Cir. 1980)).) The Court disagrees. See, e.g., United States v. An Article of Drug Consisting of 4.680 Pails, 725 F.2d 976, 985 (5th Cir. 1984) (actions brought under the Act may be decided on summary judgment where studies relied upon by drug proponent do not satisfy statutory and regulatory standards).

III. WRM-Rid is an Adulterated New Animal Drug.

A. The FDA's Case.

The Act prohibits "[t]he introduction . . . into interstate commerce of any . . . drug . . . that is adulterated." 21 U.S.C. S 331(a). Thus, to carry its burden on summary judgment under the Act, the government must show that there is no genuine issue of material fact that WRM-RID is a drug which is adulterated and which was held for sale after shipment in interstate commerce. The Court addresses the following two issues: (1) whether WRM-RID is an adulterated drug and (2) whether it has shipped in interstate commerce.

1. Adulterated Drugs

The central issue in dispute is whether WRM-RID is' adulterated. There is no dispute that WRM-RID is an animal drug within the meaning of the Act. 21 U.S.C. § 321(g) (1) (B). Therefore, the main issue is whether WRM-RID is adulterated. An adulterated drug is a "new" drug that is not the subject of either an approved application with the FDA or an effective investigational exception. 21 U.S.C. § 351(a) (5), 360b(a) (1). WRM-RID is neither the subject of an approved new animal drug application nor the subject of an effective investigational exception. Therefore, the question is whether WRM-RID is a "new" drug. The Court finds that WRM-RID is a new drug.

An animal drug is "new" under the Act if the drug is not "generally recognized as safe and effective" for use as recommended in its labeling. If the drug is a combination of drugs then the combination must be generally recognized as safe and effective even if each component part is generally recognized as safe and effective. 21 U.S.C. § 321(p) (1); 21 C.F.R. § 510.3(i) (2). International Nutrition v. United States Department of Health, 676 F.2d 338, 341 (8th Cir. 1982).

The sponsor of a drug has the burden of coming forward with substantial evidence that the drug is generally recognized as safe and effective.[1] Ubiotica Corp. v. Food and Drug Administration, 427 F.2d 376, 378 (6th Cir. 1970). This requires evidence of an "adequate and well controlled investigation supporting" the safety and effectiveness of the drug. Weinberger v. Hynson,

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[1]Bingman asserts that the FDA's motion should be denied because the FDA has failed to produce evidence that WRM-RID is unsafe. (Doc. #9 at pp. 14-15.) The FDA does not bear the burden of proof to establish that a drug is "new" under the Act; Bingman bears that burden. See, e.g., Weinberger v. Hynson, Westcott & Dunning. Inc., 412 U.S. 609, 631 (1972) (holding that the FDA may withdraw application effective prior to adoption of 1962 amendments if applicant had not provided substantial evidence of drug's efficacy). The FDA, as the party moving for summary judgment, bears the burden of showing an absence of a genuine issue of material fact. Adickes, 398 U.S. 144, 157.

Westcott & Dunning, 412 U.S. 609, 630 (1972). "Clinical impressions of practicing physicians and poorly controlled experiments" do not constitute substantial evidence. Id. at 631. Similarly, "'(i]solated case reports, random experience and reports lacking the details which permit scientific evaluation will not be considered.'" Id. at 631 (quoting 21 C.F.R. § 130.12(a) (5) (ii) (c)).

Bingman has failed to come forward with substantial evidence that WRM-RID, a combination drug, is generally recognized as safe and effective. The sponsor of a combination drug cannot show that the drug is safe and effective merely by showing that each component part is generally recognized as safe and effective; instead, the sponsor must show that the combination is safe and effective. United States v. An Article of Drugs, 513 F.2d 1127, 1129—30 (9th Cir. 1975). Where a drug sponsor cannot produce evidence of research concerning the safety and effectiveness of a drug combination, then judgment should be rendered against that party. Id. at 1129. Bingman has produced evidence that tends to establish that each of the component parts of WRM-RID -- arecoline hydrobromide and piperazine phosphate -- is generally recognized as safe and effective. (See Doc. #9 at pp. 8—14 and referenced exhibits.) The great majority of Bingman's evidence, however, fails to address the safety and effectiveness of these chemicals in combination. (Id.) The only evidence that Bingman introduces that relates to

WRM-RID as a combination drug is its 43 year "track record." (See Doc. #9 at pp. 10, 13.) This evidence is not sufficient to satisfy the "substantial evidence" test. The track record is not a well—controlled investigation and it does not contain the detail necessary to permit scientific evaluation. Therefore, this evidence does not constitute "substantial evidence."

Because there is no evidence in the record showing that WRM-RID is generally recognized as safe and effective, WRM-RID is a "new" drug. According to the foregoing evidence, therefore, WRM-RID is adulterated.

2. Interstate Commerce

The FDA may bring a condemnation proceeding against an animal drug only if the drug "is adulterated . . . when introduced into or while in interstate commerce or while held for sale . . . after shipment in interstate commerce." 21 U.S.C. § 334(a)(1). This standard is satisfied if any component of the animal drug has been shipped in interstate commerce. See, e.g., Palmer v. United States, 340 F.2d 48, 49 (5th Cir. 1964) ("Shipment of the active ingredient of a drug is the equivalent of shipping the drug."); see also 21 U.S.C. § 321(g) (1) (D) (defining "drug" to include "articles intended for use as a component of any" drug).

The FDA introduced documentary evidence establishing that both of the active ingredients in WRM-

RID, piperazine phosphate and arecoline hydrobromide, were shipped from New York to Bingman Laboratories in Ohio. (See Doc. #8 at 14—15.) Although Bingman raises the issue of interstate commerce in its answer, Bingman does not present any evidence contradicting the FDA's evidence. Therefore, there is no genuine issue of material fact with respect to the shipment of WRM-RID in interstate commerce.

The Court concludes that the FDA has met its burden on summary judgment. There is no genuine issue of material fact that WRM-RID is an adulterated animal drug that was held for sale after shipment in interstate commerce. Unless Bingman can show a genuine issue with respect to a legally recognized defense, the Court must enter judgment for the FDA.

B. Bingman's Defenses

1. Grandfather clause

Bingman argues that WRM-RID is exempt from the requirements of the Act under the 1962 grandfather clause. See 21 U.S.C. § 321 (p) (note). Therefore, Bingman asserts that it "can continue to market and sell this product with impunity." (Doc. #9 at p.7.) The Court disagrees with Bingman for two reasons.

First, even if WRM—RID satisfies the conditions of the 1962 grandfather clause, WRM—RID is only exempt from the "effectiveness" requirements of the Act. Bingman

would still be required to show that WRM-RID is generally recognized as safe. United States v. Articles of Drugs: 5906 Boxes, 745 F.2d 105, 108 (5th Cir. 1984).

Second, and more important, WRM-RID does not satisfy all of the conditions of the grandfather clause. The Act was amended in 1962 to add the "effectiveness" requirement to the definition of a "new" drug. See 21 U.S.C. § 321(p)(1) (note). The 1962 grandfather clause exempts certain drugs on the market before 1962 from the effectiveness requirement. A drug qualifies for the exemption if, in 1962, the drug, among other things, did not qualify as a "new" drug as defined by Section 201(p) of the 1938 Act. Articles of Drugs: 5906 Boxes, 745 F.2d at 108. "[T]he [1938] Act's definition of a 'new drug' before the 1962 Amendments was identical to the present definition . . . except that 'effectiveness' was not included." Id. Thus, a combination drug was "new" under the 1938 Act if the drug was not generally recognized as safe even if its component parts were recognized as safe.

Bingman has the burden of coming forward with evidence that WRM-RID, as a combination drug, was recognized in 1962 as safe. Again, Bingman has produced evidence that tends to establish that each of the component parts of WRM—RID arecoline hydrobromide and piperazine phosphate -— was generally recognized in 1962 as safe. (See Doc. #9 at pp. 8—14 and referenced exhibits.) Bingman has failed, however, to show, or even to argue,

that WRM-RID as a combination drug was generally recognized as safe in 1962. Therefore, there is no genuine issue of material fact that Bingman fails to satisfy an essential condition of the grandfather clause.

2. Due Process

Bingman asserts that the FDA violated its constitutional right to due process by seizing the WRM-RID without a hearing. This assertion is without merit because the Supreme Court has held that it is not a violation of due process for the government to seize property under the Act without holding a prior hearing. Ewing v. Mytinper & Casselberry, Inc., 339 U.S. 595, 598—600 (1950).

3. Estoppel

Bingman also suggests that its contacts with the FDA over the past 40 years and the absence of any previous enforcement action against Bingman bar this action. (See Doc. #9 at pp. 1, 8, 9.) The Court disagrees. Bingman is not entitled to a waiver to distribute illegal animal drugs because the government has not enforced the law against it previously. See Donovan v. Daniel Marr & Son, Co., 763 F.2d 477, 484 (1st Cir. 1985). The Government has a duty to correct any previous mistakes in enforcing the law it might have made. United States v. 60 28 Capsule Bottles, 211 F. Supp. 207, 215 (D. N.J. 1962), aff'd 325 F.2d 513 (3d Cir. 1963). Finally, one cannot invoke estoppel to avoid the requirements of legislation, like the Act, enacted to protect the public from products that do not comply with

the law. See Scott Paper Co. v. Marcalus Manufacturing Co., 326 U.S. 249, 257 (1945). Therefore, the Court concludes that the FDA's failure to prosecute Bingman in the past is in no way a defense to this current action.

IV. Conclusion

Upon consideration and being duly advised, the Court **GRANTS** the FDA's motion for summary judgment. The Court therefore **ORDERS** that the seized animal drug be condemned and destroyed.

IT IS SO ORDERED.

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UNITED STATES DISTRICT JUDGE

APPENDIX C

UNITED STATES COURT OF APPEALS

STATUTES

21 U.S.C. § 321
21 U.S.C. § 331
21 U.S.C. § 334
21 U.S.C. § 351
21 U.S.C. § 355

Sixth Circuit Case Nº. 97-3467

§ 321. Definitions; generally

For the purposes of this chapter -

- (a)(1) The term "State", except as used in the last sentence of section 372(a) of this title, means any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico.
    - (2) The term "Territory" means any Territory or possession of the United States, including the District of Columbia, and excluding the Commonwealth of Puerto Rico and the Canal Zone.
- (b) The term "interstate commerce" means (1) commerce between any State or Territory and any place outside thereof, and (2) commerce within the District of Columbia or within any other Territory not organized with a legislative body.
- (c) The term "Department" means Department of Health and Human Services.
- (d) The term "Secretary" means the Secretary of Health and Human Services.
- (e) The term "person" includes individual, partnership, corporation, and association.
- (f) The term "food" means (1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article.

- (g)(1) The term "drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C). A food or dietary supplement for which a claim, subject to sections 343(r)(1)(B) and 343(r)(3) of this title or sections 343(r)(1)(B) and 343(r)(5)(D) of this title, is made in accordance with the requirements of section 343(r) of this title is not a drug solely because the label or the labeling contains such a claim. A food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with section 343(r)(6) of this title is not a drug under clause (C) solely because the label or the labeling contains such a statement.
- (2) The term "counterfeit drugs" means a drug which, or the container or labeling of which, without authorization, bears the trademark, trade

name, or other identifying mark, imprint, or device, or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the person or persons who in fact manufactured, processed, packed, or distributed such drug and which thereby falsely purports or is represented to be the product of, or to have been packed or distributed by, such other drug manufacturer, processor, packer, or distributor.

- (h) The term "device" (except when used in paragraph (n) of this section and in sections 331(f), 352(c), and 362(c) of this title) means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is -
  - (1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
  - (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
  - (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on

the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

- (i) The term "cosmetic" means (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles; except that such term shall not include soap.
- (j) The term "official compendium" means the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, official National Formulary, or any supplement to any of them.
- (k) The term "label" means a display of written, printed, or graphic matter upon the immediate container of any article; and a requirement made by or under authority of this chapter that any word, statement, or other information appear on the label shall not be considered to be complied with unless such word, statement, or other information also appears on the outside container or wrapper, if any there be, of the retail package of such article, or is easily legible through the outside container or wrapper.

- (l) The term "immediate container" does not include package liners.
- (m) The term "labeling" means all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.
- (n) If an article is alleged to be misbranded because the labeling or advertising is misleading, then in determining whether the labeling or advertising is misleading there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.
- (o) The representation of a drug, in its labeling, as an antiseptic shall be considered to be a representation that it is a germicide, except in the case of a drug purporting to be, or represented as, an antiseptic for inhibitory use as a wet dressing,

ointment, dusting powder, or such other use as involves prolonged contact with the body.

- (p) The term "new drug" means -
  - (1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to June 25, 1938, it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or
  - (2) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material

extent or for a material time under such conditions.

- (q) The term "pesticide chemical" means any substance which, alone, in chemical combination or in formulation with one or more other substances, is "a pesticide" within the meaning of the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq.) as now in force or as hereafter amended, and which is used in the production, storage, or transportation of raw agricultural commodities.
- (r) The term "raw agricultural commodity" means any food in its raw or natural state, including all fruits that are washed, colored, or otherwise treated in their unpeeled natural form prior to marketing.
- (s) The term "food additive" means any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been

adequately shown through scientific procedures (or, in the case as a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; except that such term does not include -

- (1) a pesticide chemical in or on a raw agricultural commodity; or
- (2) a pesticide chemical to the extent that it is intended for use or is used in the production, storage, or transportation of any raw agricultural commodity; or
- (3) a color additive; or
- (4) any substance used in accordance with a sanction or approval granted prior to September 6, 1958, pursuant to this chapter, the Poultry Products Inspection Act (21 U.S.C. 451 et seq.) or the Meat Inspection Act of March 4, 1907, as amended and extended (21 U.S.C. 601 et seq.);
- (5) a new animal drug; or
- (6) an ingredient described in paragraph (if) in, or intended for use in, a dietary supplement.

- (t)(1) The term "color additive" means a material which -
  - (A) is a dye, pigment, or other substance made by a process of synthesis or similar

artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source, and

- (B) when added or applied to a food, drug, or cosmetic, or to the human body or any part thereof, is capable (alone or through reaction with other substance) of imparting color thereto; except that such term does not include any material which the Secretary, by regulation, determines is used (or intended to be used) solely for a purpose or purposes other than coloring.

- (2) The term "color" includes black, white, and intermediate grays.
- (3) Nothing in subparagraph (1) of this paragraph shall be construed to apply to any pesticide chemical, soil or plant nutrient, or other agricultural chemical solely because of its effect in aiding, retarding, or otherwise affecting, directly or indirectly, the growth or other natural physiological processes of produce of the soil and thereby affecting its color, whether before or after harvest.

- (u) The term "safe" as used in paragraph(s) of this section and in sections 348, 360b, and 379e of this title, has reference to the health of man or animal.

- (v) The term "new animal drug" means any drug intended for use for animals other than man, including any drug intended for use in animal feed but not including such animal feed, -
  - (1) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new animal drug" if at any time prior to June 25, 1938, it was subject to the Food and Drug Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or
  - (2) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.
- (w) The term "animal feed", as used in paragraph (w) (FOOTNOTE 1) of this section,

in section 360b of this title, and in provisions of this chapter referring to such paragraph or section, means an article which is intended for use for food for animals other than man and which is intended for use as a substantial source of nutrients in the diet of the animal, and is not limited to a mixture intended to be the sole ration of the animal.

(FOOTNOTE 1) So in original. Probably should be paragraph "(v)".

- (x) The term "informal hearing" means a hearing which is not subject to section 554, 556, or 557 of title 5 and which provides for the following:
  - (1) The presiding officer in the hearing shall be designated by the Secretary from officers and employees of the Department who have not participated in any action of the Secretary which is the subject of the hearing and who are not directly responsible to an officer or employee of the Department who has participated in any such action.
  - (2) Each party to the hearing shall have the right at all times to be advised and accompanied by an attorney.
  - (3) Before the hearing, each party to the hearing shall be given reasonable notice of the matters

to be considered at the hearing, including a comprehensive statement of the basis for the action taken or proposed by the Secretary which is the subject of the hearing and a general summary of the information which will be presented by the Secretary at the hearing in support of such action.

- (4) At the hearing the parties to the hearing shall have the right to hear a full and complete statement of the action of the Secretary which is the subject of the hearing together with the information and reasons supporting such action, to conduct reasonable questioning, and to present any oral or written information relevant to such action.
- (5) The presiding officer in such hearing shall prepare a written report of the hearing to which shall be attached all written material presented at the hearing. The participants in the hearing shall be given the opportunity to review and correct or supplement the presiding officer's report of the hearing.
- (6) The Secretary may require the hearing to be transcribed. A party to the hearing shall have the right to have the hearing transcribed at his expense. Any transcription of a hearing shall

be included in the presiding officer's report of the hearing.

- (y) The term "saccharin" includes calcium saccharin, sodium saccharin, and ammonium saccharin.
- (z) The term "infant formula" means a food which purports to be or is represented for special dietary use solely as a food for infants by reason of its simulation of human milk or its suitability as a complete or partial substitute for human milk.
  - (aa) The term "abbreviated drug application" means an application submitted under section 355(j) or 357 of this title for the approval of a drug that relies on the approved application of another drug with the same active ingredient to establish safety and efficacy, and -
    - (1) in the case of section 335a of this title, includes a supplement to such an application for a different or additional use of the drug but does not include a supplement to such an application for other than a different or additional use of the drug, and
    - (2) in the case of sections 335b and 335c of this title, includes any supplement to such an application.
  - (bb) The term "knowingly" or "knew" means that a person, with respect to information -

- (1) has actual knowledge of the information, or
- (2) acts in deliberate ignorance or reckless disregard of the truth or falsity of the information.

- (cc) For purposes of section 335a of this title, the term "high managerial agent" -
  - (1) means—
    - (A) an officer or director of a corporation or an association,
    - (B) a partner of a partnership, or
    - (C) any employee or other agent of a corporation, association, or partnership, having duties such that the conduct of such officer, director, partner, employee, or agent may fairly be assumed to represent the policy of the corporation, association, or partnership, and
  - (2) includes persons having management responsibility for -
    - (A) submissions to the Food and Drug Administration regarding the development or approval of any drug product,
    - (B) production, quality assurance, or quality control of any drug product, or

- (C) research and development of any drug product.

- (dd) For purposes of sections 335a and 335b of this title, the term "drug product" means a drug subject to regulation under section 355, 357, 360b, or 382 of this title or under section 262 of title 42.
- (ee) The term "Commissioner" means the Commissioner of Food and Drugs.
- (ff) The term "dietary supplement" -
  - (1) means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:
    - (A) a vitamin;
    - (B) a mineral;
    - (C) an herb or other botanical;
    - (D) an amino acid;
    - (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or
    - (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E);
  - (2) means a product that -

- (A)(i) is intended for ingestion in a form described in section 350(c)(1)(B)(ii) of this title; or (ii) complies with section 350(c)(1)(B)(ii) of this title;
- (B) is not represented for use as a conventional food or as a sole item of a meal or the diet; and
- (C) is labeled as a dietary supplement; and

- (3) does-
  - (A) include an article that is approved as a new drug under section 355 of this title, certified as an antibiotic under section 357 of this title, or licensed as a biologic under section 262 of title 42 and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary has issued a regulation, after notice and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages set forth in the labeling for such dietary supplement, is unlawful under section 342(f) of this title; and
  - (B) not include -

- (i) an article that is approved as a new drug under section 355 of this title, certified as an antibiotic under section 357 of this title, or licensed as a biologic under section 262 of title 42, or
- (ii) an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this chapter. Except for purposes of paragraph (g), a dietary supplement shall be deemed to be a food within the meaning of this chapter.

§ 331. Prohibited acts

The following acts and the causing thereof are prohibited:

- (a) The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.
- (b) The adulteration or misbranding of any food, drug, device, or cosmetic in interstate commerce.
- (c) The receipt in interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise.
- (d) The introduction or delivery for introduction into interstate commerce of any article in violation of section 344 or 355 of this title.
- (e) The refusal to permit access to or copying of any record as required by section 350a or 373 of this title; or the failure to establish or maintain any record, or make any report, required under section 350a, 355(i) or (k), 357(d) or (g), 360b(a)(4)(C), 360b(j), (l), or (m), 360e(f), or 360i of this title, or the refusal to permit access to or verification or copying of any such required record.
- (f) The refusal to permit entry or inspection as authorized by section 374 of this title.
- (g) The manufacture within any Territory of any food, drug, device, or cosmetic that is adulterated or misbranded.

- (h) The giving of a guaranty or undertaking referred to in section 333(c)(2) of this title, which guaranty or undertaking is false, except by a person who relied upon a guaranty or undertaking to the same effect signed by, and containing the name and address of, the person residing in the United States from whom he received in good faith the food, drug, device, or cosmetic; or the giving of a guaranty or undertaking referred to in section 333(c)(3) of this title, which guaranty or undertaking is false.
- (i)(1) Forging, counterfeiting, simulating, or falsely representing, or without proper authority using any mark, stamp, tag, label, or other identification device authorized or required by regulations promulgated under the provisions of section 344, 356, 357, or 379e of this title.
    - (2) Making, selling, disposing of, or keeping in possession, control, or custody, or concealing any punch, die, plate, stone, or other thing designed to print, imprint, or reproduce the trademark, trade name, or other identifying mark, imprint, or device of another or any likeness of any of the foregoing upon any drug or container or labeling thereof so as to render such drug a counterfeit drug.

- (3) The doing of any act which causes a drug to be a counterfeit drug, or the sale or dispensing, or the holding for sale or dispensing, of a counterfeit drug.

- (j) The using by any person to his own advantage, or revealing, other than to the Secretary or officers or employees of the Department, or to the courts when relevant in any judicial proceeding under this chapter, any information acquired under authority of section 344, 348, 350a, 355, 356, 357, 360, 360b, 360c, 360d, 360e, 360f, 360h, 360i, 360j, 374, 379, or 379e of this title concerning any method or process which as a trade secret is entitled to protection. This paragraph does not authorize the withholding of information from either House of Congress or from, to the extent of matter within its jurisdiction, any committee or subcommittee of such committee or any joint committee of Congress or any subcommittee of such joint committee.

- (k) The alteration, mutilation, destruction, obliteration, or removal of the whole or any part of the labeling of, or the doing of any other act with respect to, a food, drug, device, or cosmetic, if such act is done while such article is held for sale (whether or not the first sale) after shipment in interstate commerce and results in such article being adulterated or misbranded.

- (l) The using, on the labeling of any drug or device or in any advertising relating to such drug or device, of any representation or suggestion that approval of an application with respect to such drug or device is in effect under section 355, 360e, or 360i(g) of this title, as the case may be, or that such drug or device complies with the provisions of such section.
- (m) The sale or offering for sale of colored oleomargarine or colored margarine, or the possession or serving of colored oleomargarine or colored margarine in violation of subsections (b) or (c) of section 347 of this title.
- (n) The using, in labeling, advertising or other sales promotion of any reference to any report or analysis furnished in compliance with section 374 of this title.
- (o) In the case of a prescription drug distributed or offered for sale in interstate commerce, the failure of the manufacturer, packer, or distributor thereof to maintain for transmittal, or to transmit, to any practitioner licensed by applicable State law to administer such drug who makes written request for information as to such drug, true and correct copies of all printed matter which is required to be included in any package in which that drug is distributed or sold, or such other printed matter as is approved by the Secretary. Nothing in this

paragraph shall be construed to exempt any person from any labeling requirement imposed by or under other provisions of this chapter.

- (p) The failure to register in accordance with section 360 of this title, the failure to provide any information required by section 360(j) or 360(k) of this title, or the failure to provide a notice required by section 360(j)(2) of this title.
- (q)(1) The failure or refusal to (A) comply with any requirement prescribed under section 360h or 360j(g) of this title, (B) furnish any notification or other material or information required by or under section 360i or 360j(g) of this title, or (C) comply with a requirement under section 360l of this title.
  - (2) With respect to any device, the submission of any report that is required by or under this chapter that is false or misleading in any material respect.
- (r) The movement of a device in violation of an order under section 334(g) of this title or the removal or alteration of any mark or label required by the order to identify the device as detained.
- (s) The failure to provide the notice required by section 350a(c) or 350a(e) of this title, the failure to make the reports required by section 350a(f)(1)(B) of this title, the failure to retain the records required by section 350a(b)(4) of this title, or the failure to

meet the requirements prescribed under section 350a(f)(3) of this title.

- (t) The importation of a drug in violation of section 381(d)(1) of this title, the sale, purchase, or trade of a drug or drug sample or the offer to sell, purchase, or trade a drug or drug sample in violation of section 353(c) of this title, the sale, purchase, or trade of a coupon, the offer to sell, purchase, or trade such a coupon, or the counterfeiting of such a coupon in violation of section 353(c)(2) of this title, the distribution of a drug sample in violation of section 353(d) of this title or the failure to otherwise comply with the requirements of section 353(d) of this title, or the distribution of drugs in violation of section 353(e) of this title or the failure to otherwise comply with the requirements of section 353(e) of this title.
- (u) The failure to comply with any requirements of the provisions of, or any regulations or orders of the Secretary, under section 360b(a)(4)(A), 360(a)(4)(D), or 360b(a)(5) of this title. (u) (FOOTNOTE 1) The introduction or delivery for introduction into interstate commerce of a dietary supplement that is unsafe under section 350b of this title.

(FOOTNOTE 1) So in original. Probably should be "(v)".

§ 334. Seizure

- (a) Grounds and jurisdiction
  - (1) Any article of food, drug, or cosmetic that is adulterated or misbranded when introduced into or while in interstate commerce or while held for sale (whether or not the first sale) after shipment in interstate commerce, or which may not, under the provisions of section 344 or 355 of this title, be introduced into interstate commerce, shall be liable to be proceeded against while in interstate commerce, or at any time thereafter, on libel of information and condemned in any district court of the United States or United States court of a Territory within the jurisdiction of which the article is found. No libel for condemnation shall be instituted under this chapter, for any alleged misbranding if there is pending in any court a libel for condemnation proceeding under this chapter based upon the same alleged misbranding, and not more than one such proceeding shall be instituted if no such proceeding is so pending, except that such limitations shall not apply (A) when such misbranding has been the basis of a prior judgment in favor of the United States, in a criminal, injunction, or libel for condemnation

proceeding under this chapter, or (B) when the Secretary has probable cause to believe from facts found, without hearing, by him or any officer or employee of the Department that the misbranded article is dangerous to health, or that the labeling of the misbranded article is fraudulent, or would be in a material respect misleading to the injury or damage of the purchaser or consumer. In any case where the number of libel for condemnation proceedings is limited as above provided the proceeding pending or instituted shall, on application of the claimant, seasonably made, be removed for trial to any district agreed upon by stipulation between the parties, or, in case of failure to so stipulate within a reasonable time, the claimant may apply to the court of the district in which the seizure has been made, and such court (after giving the United States attorney for such district reasonable notice and opportunity to be heard) shall by order, unless good cause to the contrary is shown, specify a district of reasonable proximity to the claimant's principal place of business, to which the case shall be removed for trial.

(2) The following shall be liable to be proceeded against at any time on libel of

information and condemned in any district court of the United States or United States court of a Territory within the jurisdiction of which they are found: (A) Any drug that is a counterfeit drug, (B) Any container of a counterfeit drug, (C) Any punch, die, plate, stone, labeling, container, or other thing used or designed for use in making a counterfeit drug or drugs, and (D) Any adulterated or misbranded device.

- (3)(A) Except as provided in subparagraph (B), no libel for condemnation may be instituted under paragraph (1) or (2) against any food which -
  - (i) is misbranded under section 343(a)(2) of this title because of its advertising, and
  - (ii) is being held for sale to the ultimate consumer in an establishment other than an establishment owned or operated by a manufacturer, packer, or distributor of the food.
- (B) A libel for condemnation may be instituted under paragraph (1) or (2) against a food described in subparagraph (A) if-
  - (i)(I) the food's advertising which resulted in the food being misbranded under section 343(a)(2) of this title was

disseminated in the establishment in which the food is being held for sale to the ultimate consumer, (II) such advertising was disseminated by, or under the direction of, the owner or operator of such establishment, or (III) all or part of the cost of such advertising was paid by such owner or operator; and

- (ii) the owner or operator of such establishment used such advertising in the establishment to promote the sale of the food.

- (b) Procedure; multiplicity of pending proceedings The article, equipment, or other thing proceeded against shall be liable to seizure by process pursuant to the libel, and the procedure in cases under this section shall conform, as nearly as may be, to the procedure in admiralty; except that on demand of either party any issue of fact joined in any such case shall be tried by jury. When libel for condemnation proceedings under this section, involving the same claimant and the same issues of adulteration or misbranding, are pending in two or more jurisdictions, such pending proceedings, upon application of the claimant seasonably made to the court of one such jurisdiction, shall be consolidated

for trial by order of such court, and tried in (1) any district selected by the claimant where one of such proceedings is pending; or (2) a district agreed upon by stipulation between the parties. If no order for consolidation is so made within a reasonable time, the claimant may apply to the court of one such jurisdiction and such court (after giving the United States attorney for such district reasonable notice and opportunity to be heard) shall by order, unless good cause to the contrary is shown, specify a district of reasonable proximity to the claimant's principal place of business, in which all such pending proceedings shall be consolidated for trial and tried. Such order of consolidation shall not apply so as to require the removal of any case the date for trial of which has been fixed. The court granting such order shall give prompt notification thereof to the other courts having jurisdiction of the cases covered thereby.

- (c) Availability of samples of seized goods prior to trial

  The court at any time after seizure up to a reasonable time before trial shall by order allow any party to a condemnation proceeding, his attorney or agent, to obtain a representative sample of the article seized and a true copy of the analysis, if any, on which the proceeding is based and the identifying

marks or numbers, if any, of the packages from which the samples analyzed were obtained.

- (d) Disposition of goods after decree of condemnation; claims for remission or mitigation of forfeitures
  - (1) Any food, drug, device, or cosmetic condemned under this section shall, after entry of the decree, be disposed of by destruction or sale as the court may, in accordance with the provisions of this section, direct and the proceeds thereof, if sold, less the legal costs and charges, shall be paid into the Treasury of the United States; but such article shall not be sold under such decree contrary to the provisions of this chapter or the laws of the jurisdiction in which sold. After entry of the decree and upon the payment of the costs of such proceedings and the execution of a good and sufficient bond conditioned that such article shall not be sold or disposed of contrary to the provisions of this chapter or the laws of any State or Territory in which sold, the court may by order direct that such article be delivered to the owner thereof to be destroyed or brought into compliance with the provisions of this chapter, under the supervision of an officer or employee duly designated by the Secretary, and the expenses of

such supervision shall be paid by the person obtaining release of the article under bond. If the article was imported into the United States and the person seeking its release establishes (A) that the adulteration, misbranding, or violation did not occur after the article was imported, and (B) that he had no cause for believing that it was adulterated, misbranded, or in violation before it was released from customs custody, the court may permit the article to be delivered to the owner for exportation in lieu of destruction upon a showing by the owner that all of the conditions of section 381(e) of this title can and will be met. The provisions of this sentence shall not apply where condemnation is based upon violation of section 342(a)(1), (2), or (6), section 351(a)(3), section 352(j), or section 361(a) or (d) of this title. Where such exportation is made to the original foreign supplier, then paragraphs (1) and (2) of section 381(e) of this title and the preceding sentence shall not be applicable; and in all cases of exportation the bond shall be conditioned that the article shall not be sold or disposed of until the applicable conditions of section 381(e) of this title have been met. Any article condemned by reason of its being an article

which may not, under section 344 or 355 of this title, be introduced into interstate commerce, shall be disposed of by destruction.

- (2) The provisions of paragraph (1) of this subsection shall, to the extent deemed appropriate by the court, apply to any equipment or other thing which is not otherwise within the scope of such paragraph and which is referred to in paragraph (2) of subsection (a) of this section.
- (3) Whenever in any proceeding under this section, involving paragraph (2) of subsection (a) of this section, the condemnation of any equipment or thing (other than a drug) is decreed, the court shall allow the claim of any claimant, to the extent of such claimant's interest, for remission or mitigation of such forfeiture if such claimant proves to the satisfaction of the court (i) that he has not committed or caused to be committed any prohibited act referred to in such paragraph (2) and has no interest in any drug referred to therein, (ii) that he has an interest in such equipment or other thing as owner or lienor or otherwise, acquired by him in good faith, and (iii) that he at no time had any knowledge or reason to believe that such equipment or other

thing was being or would be used in, or to facilitate, the violation of laws of the United States relating to counterfeit drugs.

- (e) Costs

  When a decree of condemnation is entered against the article, court costs and fees, and storage and other proper expenses, shall be awarded against the person, if any, intervening as claimant of the article.

- (f) Removal of case for trial

  In the case of removal for trial of any case as provided by subsection (a) or (b) of this section-

  - (1) The clerk of the court from which removal is made shall promptly transmit to the court in which the case is to be tried all records in the case necessary in order that such court may exercise jurisdiction.
  - (2) The court to which such case was removed shall have the powers and be subject to the duties, for purposes of such case, which the court from which removal was made would have had, or to which such court would have been subject, if such case had not been removed.

- (g) Administrative restraint; detention orders

(1) If during an inspection conducted under section 374 of this title of a facility or a vehicle, a device which the officer or employee making the inspection has reason to believe is adulterated or misbranded is found in such facility or vehicle, such officer or employee may order the device detained (in accordance with regulations prescribed by the Secretary) for a reasonable period which may not exceed twenty days unless the Secretary determines that a period of detention greater than twenty days is required to institute an action under subsection (a) of this section or section 332 of this title, in which case he may authorize a detention period of not to exceed thirty days. Regulations of the Secretary prescribed under this paragraph shall require that before a device may be ordered detained under this paragraph the Secretary or an officer or employee designated by the Secretary approve such order. A detention order under this paragraph may require the labeling or marking of a device during the period of its detention for the purpose of identifying the device as detained. Any person who would be entitled to claim a device if it were seized under subsection (a) of this section may appeal to the Secretary a

detention of such device under this paragraph. Within five days of the date an appeal of a detention is filed with the Secretary, the Secretary shall after affording opportunity for an informal hearing by order confirm the detention or revoke it.

- (2)(A) Except as authorized by subparagraph (B), a device subject to a detention order issued under paragraph (1) shall not be moved by any person from the place at which it is ordered detained until -
    - (i) released by the Secretary, or
    - (ii) the expiration of the detention period applicable to such order, whichever occurs first.
- (B) A device subject to a detention order under paragraph (1) may be moved -
    - (i) in accordance with regulations prescribed by the Secretary, and
    - (ii) if not in final form for shipment, at the discretion of the manufacturer of the device for the purpose of completing the work required to put it in such form.

§ 351. Adulterated drugs and devices

A drug or device shall be deemed to be adulterated -

- (a) Poisonous, insanitary, etc., ingredients; adequate controls in manufacture
  - (1) If it consists in whole or in part of any filthy, putrid, or decomposed substance; or (2)(A) if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health; or (B) if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess; or (3) if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health; or (4) if(A) it bears or contains, for purposes of coloring only, a color additive which is unsafe within the meaning of section 379e(a) of this title, or (B) it is a color additive

the intended use of which in or on drugs or devices is for purposes of coloring only and is unsafe within the meaning of section 379e(a) of this title; or (5) if it is a new animal drug which is unsafe within the meaning of section 360b of this title; or (6) if it is an animal feed bearing or containing a new animal drug, and such animal feed is unsafe within the meaning of section 360b of this title.

- (b) Strength, quality, or purity differing from official compendium

  If it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, the standard set forth in such compendium. Such determination as to strength, quality, or purity shall be made in accordance with the tests or methods of assay set forth in such compendium, except that whenever tests or methods of assay have not been prescribed in such compendium, or such tests or methods of assay as are prescribed are, in the judgment of the Secretary, insufficient for the making of such determination, the Secretary shall bring such fact to the attention of the appropriate body charged with the revision of such compendium, and if such body fails within a reasonable time to prescribe tests or

methods of assay which, in the judgment of the Secretary, are sufficient for purposes of this paragraph, then the Secretary shall promulgate regulations prescribing appropriate tests or methods of assay in accordance with which such determination as to strength, quality, or purity shall be made. No drug defined in an official compendium shall be deemed to be adulterated under this paragraph because it differs from the standard of strength, quality, or purity therefor set forth in such compendium, if its difference in strength, quality, or purity from such standard is plainly stated on its label. Whenever a drug is recognized in both the United States Pharmacopoeia and the Homeopathic Pharmacopoeia of the United States it shall be subject to the requirements of the United States Pharmacopoeia unless it is labeled and offered for sale as a homeopathic drug, in which case it shall be subject to the provisions of the Homeopathic Pharmacopoeia of the United States and not to those of the United States Pharmacopoeia.

- (c) Misrepresentation of strength, etc., where drug is unrecognized in compendium

  If it is not subject to the provisions of paragraph (b) of this section and its strength differs from, or its

purity or quality falls below, that which it purports or is represented to possess.

- (d) Mixture with or substitution of another substance
  If it is a drug and any substance has been (1) mixed or packed therewith so as to reduce its quality or strength or (2) substituted wholly or in part therefor.
- (e) Devices not in conformity with performance standards
  If it is, or purports to be or is represented as, a device which is subject to a performance standard established under section 360d of this title unless such device is in all respects in conformity with such standard.
- (f) Certain class III devices
  - (1) If it is a class III device -
    - (A)(i) which is required by a regulation promulgated under subsection (b) of section 360e of this title to have an approval under such section of an application for premarket approval and which is not exempt from section 360e of this title under section 3601(g) of this title, and
    - (ii)(I) for which an application for premarket approval or a notice of completion of a product development protocol was not filed with the Secretary within the ninety-day period beginning on

the date of the promulgation of such regulation, or (II) for which such an application was filed and approval of the application has been denied, suspended, or withdrawn, or such a notice was filed and has been declared not completed or the approval of the device under the protocol has been withdrawn; (B)(i) which was classified under section 360c(f) of this title into class III, which under section 360e(a) of this title is required to have in effect an approved application for premarket approval, and which is not exempt from section 360e of this title under section 3601(g) of this title, and (ii) which has an application which has been suspended or is otherwise not in effect; or (C) which was classified under section 360j(l) of this title into class III, which under such section is required to have in effect an approved application under section 360e of this title, and which has an application which has been suspended or is otherwise not in effect. (2)(A) In the case of a device classified under section 360c(f) of this title into class III and intended solely for investigational use, paragraph (FOOTNOTE

1) (1)(B) shall not apply with respect to such device during the period ending on the ninetieth day after the date of the promulgation of the regulations prescribing the procedures and conditions required by section 360j(g)(2) of this title.

(FOOTNOTE 1) So in original. Probably should be "subparagraph". (B) In the case of a device subject to a regulation promulgated under subsection (b) of section 360e of this title, paragraph

(FOOTNOTE 1) (1) shall not apply with respect to such device during the period ending -

- (i) on the last day of the thirtieth calendar month beginning after the month in which the classification of the device in class III became effective under section 360c of this title, or
- (ii) on the ninetieth day after the date of the promulgation of such regulation, whichever occurs later.

- (g) Banned devices

  If it is a banned device.

- (h) Manufacture, packing, storage, or installation of device not in conformity with applicable requirements or conditions

  If it is a device and the methods used in, or the facilities or controls used for, its manufacture, packing, storage, or installation are not in conformity with applicable requirements under section 360j(f)(1) of this title or an applicable condition prescribed by an order under section 360i(f)(2) of this title.
- (i) Failure to comply with requirements under which device was exempted for investigational use

  If it is a device for which an exemption has been granted under section 360j(g) of this title for investigational use and the person who was granted such exemption or any investigator who uses such device under such exemption fails to comply with a requirement prescribed by or under such section.

§ 355. New drugs

- (a) Necessity of effective approval of application
  No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.
- (b) Filing application; contents
  - (1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (F) specimens of the labeling proposed to be used for such drug. The applicant shall file with the application the patent number and the expiration date of any

patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences.

- (2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include -

- (A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section -
  - (i) that such patent information has not been filed,
  - (ii) that such patent has expired,
  - (iii) of the date on which such patent will expire, or
  - (iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and
- (B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a

statement that the method of use patent does not claim such a use.

- (3)(A) An applicant who makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give the notice required by subparagraph
  - (B)to
    - (i) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and
    - (ii) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice. (B) The notice referred to in subparagraph (A) shall state that an application has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed

statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

- (C) If an application is amended to include a certification described in paragraph (2)(A)(iv), the notice required by subparagraph (B) shall be given when the amended application is submitted.

- (c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order
  - (1) Within one hundred and eighty days after the filing of an application under subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either -
    - (A) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or
    - (B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after

such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file

patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

- (3) The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined under the following:
  - (A) If the applicant only made a certification describIf the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) of this section or in both such clauses
  - (B) If the applicant made a certification described in clause (iii) of subsection

(b)(2)(A) of this section, the approval may be made effective on the date certified under clause (iii).

- (C) If the applicant made a certification described in clause

- (iv) of subsection (b)(2)(A) of this section, the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (3)(B) is received. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (3)(B) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that -
    - (i) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval may be made effective on the date of the court decision,
    - (ii) if before the expiration of such period the court decides that such patent

has been infringed, the approval may be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or

- (iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision. In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (3)(B) is received, no action may be brought under section 2201 of title 28 for a declaratory judgment with respect to the patent. Any action brought under such section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of

business. (D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration often years from the date of the approval of the application previously approved under subsection (b) of this section. (ii) If an application submitted under subsection

(b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b)

application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application. (iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations

(other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

- (iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailabilty (FOOTNOTE

i) studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(FOOTNOTE 1) So in original. Probably should be "bioavailability".

• (v) If an application (or supplement to an applicIf an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active

ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expi

- (d) Grounds for refUsing application; approval of application; "substantial evidence" defined

  If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that

- (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof, (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the

conditions of use prescribed, recommended, or suggested in the proposed labeling thereof, or (6) the application failed to contain the patent information prescribed by subsection (b) of this section; or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof

- (e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

  The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or

suggested in the labeling thereof, or (4) the patent information prescribed by subsection (c) of this section was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: Provided, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) of this section with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has

refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of, or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of Any order under this subsection shall state the findings upon which it is based.

- (f) Revocation of order refusing, withdrawing or suspending approval of application

  Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) of this section refUsing,

withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

- (g) Service of orders

  Orders of the Secretary issued under this section shall be served

  - (1) in person by any officer or employee of the department designated by the Secretary or

    (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

- (h) Appeal from order

  An appeal may be taken by the applicant from an order of the Secretary refUsing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals or the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify

and file in the court the record upon which the order complained of was entered, as provided in section 2112 of title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the

setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification of title 28. Upon the f1254 of title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

- (i) Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon -
  - (1) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

- (2) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings; and
- (3) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b) of this section. Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or

sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.

- (j) Abbreviated new drug applications
  - (1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.
  - (2)(A) An abbreviated application for a new drug shall contain -
    - (i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (6) (hereinafter in this subsection referred to as a "listed drug");

- (ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug; (II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or (III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

- (iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;
- (iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

- (v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;
- (vi) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;
- (vii) a certification, in the opinion of the applicaa certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section - (I) that such patent information has not been filed, (II) that such patent has expired, (III) of the date on which such patent will expire, or (IV) that such patent is invalid or will not be

infringed by the manufacture, use, or sale of the new dru

- (viii) if with respect to the listed drug referred to in clause
  - (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use. The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).
- (B)(i) An applicant who makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give the notice required by clause (ii) to - (I) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and (II) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the

patent or the representative of such holder designated to receive such notice. (ii) The notice referred to in clause (i) shall state that an application, which contains data from bioavailability or bioequivalence studies, has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

- (iii) If an application is amended to include a certification described in subparagraph (A)(vii)(IV), the notice required by clause (ii) shall be given when the amended application is submitted. (C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The

Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds -

- (i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or
- (ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

- (3) Subject to paragraph (4), the Secretary shall approve an application for a drug unless the Secretary finds -
  - (A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;
  - (B) information submitted with the application is insufficient to show that each

of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

- (C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug; (ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or (iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show - (I) that the other active ingredients are the same as the active ingredients of the listed drug, or (II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title, or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

- (D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or (ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);
- (E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;
- (F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to

in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

- (G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;
- (H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed,

recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

- (I) the approval under subsection (c) of this section of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section, the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) of this section for grounds described in the first sentence of subsection (e) of this section, the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (5), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;
- (J) the application does not meet any other requirement of paragraph (2)(A); or

- (K) the application contains an untrue statement of material fact.

- (4)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.
  - (B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable dateThe approval of an application su
    - (i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.
    - (ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).
    - (iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless an action is brought for infringement of

a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that - (I) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision, (II) if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or (III) if before the expiration of such period the court grants a preliminary injunction

prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision. In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of title 28, for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

- (iv) If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this

subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after - (I) the(2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after - (I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of

- (C) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an

expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

- (D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b) of this section. (ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved

after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application. (iii) If an application submitted under subsection (b)

of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the

approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a swhich includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which

the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years fr

- (A) for the same period as the withdrawal or suspension under subsection (e) of this section or this paragraph, or
- (B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

- (6)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public - (I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) of this section before September 24, 1984; (II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and (III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published. (ii) Every thirty days after the

publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) of this section or approved under this subsection during the thirty-day period. (iii) When patent information submitted under subsection (b) or (c) of this section respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

- (B) A drug approved for safety and effectiveness under subsection (c) of this section or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.
- (C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under paragraph (5) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A)

or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list -

- (i) for the same period as the withdrawal or suspension under subsection (e) of this section or paragraph (5), or
- (ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons. A notice of the removal shall be published in the Federal Register.

- (7) For purposes of this subsection:
  - (A) The term "bioavailability" means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.
  - (B) A drug shall be considered to be bioequivalent to a listed drug if-
    - (i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when

administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

- (ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

- (8) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of -
  - (A) the name of the applicant,
  - (B) the name of the drug covered by the application,
  - (C) the name of each person to whom the review of the chemistry of the application

was assigned and the date of such assignment, and

- (D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment. The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

- (k) Records and reports; required information; regulations and orders; access to records
  - (1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) of this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or

may be ground for invoking subsection (e) of this section. Regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

- (2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

- (l) Public disclosure of safety and effectiveness data Safety and effectiveness data and information which has been submitted in an application under subsection (b) of this section for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown
  - (1) if no work is being or will be undertaken to have the application approved,

- (2) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,
- (3) if approval of the application under subsection (c) of this section is withdrawn and all legal appeals have been exhausted,
- (4) if the Secretary has determined that such drug is not a new drug, or
- (5) upon the effective date of the approval of the first application under subsection (I) of this section which refers to such drug or upon the date upon which the approval of an application under subsection (j) of this section which refers to such drug could be made effective if such an application had been submitted.

- (m) "Patent" defined

  For purposes of this section, the term "patent" means a patent issued by the Patent and Trademark Office of the Department of Commerce.

APPENDIX D

UNITED STATES COURT OF APPEALS
FOR THE SOUTHERN DISTRICT OF OHIO
EASTERN DIVISION

AFFIDAVIT OF WILLIAM SEMPLE,
PRESIDENT AND GENERAL MANAGER
OF BINGMAN LABORATORIES, INC.

Sixth Circuit Case Nº. 97-3467

IN THE DISTRICT COURT OF THE UNITED STATES
FOR THE SOUTHERN DISTRICT OF OHIO
EASTERN DIVISION

UNITED STATES OF AMERICA,
Plaintiff,

Civil Action
No. C2-94-725

v.

Judge Beckwith

Magistrate Judge Kemp

UNDETERMINED QUANTITIES
OF BAGS OF AN ARTICLE OF DRUG
FOR VETERINARY USE, ETC.

AFFIDAVIT OF WILLIAM D. SEMPLE, PRESIDENT AND GENERAL MANAGER OF BINGMAN LABORATORIES. INC.

STATE OF FLORIDA :
: ss.
COUNTY OF CITRUS :

I, William D. Semple, being first duly cautioned and sworn, state that the following facts are true to the best of my personal knowledge and belief.

1. That I am the President and General Manager of Bingman Laboratories, Inc. ("Bingman");

2. That I have approximately 43 years of experience with the production, formulation, research, and

study regarding the efficacy and safety of WRM-RID. Over this period of time, I have met no other person or veterinarian doctor who has the knowledge and experience that I have with this particular product.

3. That Bingman began marketing "WRM-RID" in 1952. Prior to placing WRM-RID on the market, I contacted Dr. Moskey, Veterinary Medical Director of the FDA, and Dr. J.H. Collins, Assistant Veterinary Medical Director, both of whom advised me that Bingman was not required to submit any information on WRM-RID. Dr. Collins did tell me, however, that if Bingman did, in fact, submit formula and label copy, they would be willing to review the material and make certain recommendations. (See "Exhibit A.") In light of this request, I sent to Collins the WRM-RID formulations and labels to which he made several suggestions. I incorporated his comments in the formulation and labels of the product. Once done, neither Dr. Moskey nor Dr. J.H. Collins took exception to the marketing of WRM-RID.

4. That in 1955, "WRM-RID" was reformulated to replace santonin with piperazine because piperazine was an FDA newly approved and much more effective anthelmintic. From 1955 through 1991, the FDA made several inspections of the Bingman plant; however, the FDA never once took exception to the labelling of WRM-RID or commented on its safety or efficacy.

5. That from 1955, WRM-RID has not undergone a single change in formulation, i.e., Bingman has never altered the percentage of active ingredients, the labeling claims, including the instructions for use; or any part of the manufacturing process. Significantly, WRM-RID has been used for over 43 years to treat approximately 3,000,0000 dogs and cats with only five complaints regarding toxicity. Copies of the Current label and instructions for use are attached hereto as "Exhibit B."

6. That in November of 1951, Dr. H.E. Moskey, V.M.D., the then Director of Veterinary Medicine, wrote me a letter (See "Exhibit C") in which he said the following:

> According to the best information we have been able to obtain from parasitologists of the Division of Zoology, Bureau of Animal Industry of the U. S. Department of Agriculture, arecoline hydrobromide in doses of 1/8 grain to small dogs, 1/4 grain to dogs of medium size, and 1/2 grain to large dogs appears to be fairly effective in removing the various species of tapeworms which infest dogs.

7. That on November 30, 1967 the FDA issued its own Intra-Office Memorandum (See Exhibit "D") stating that Adams No-Mo Dog Worm Expeller, an arecoline-based product like WRM-RID, was both safe and effective.

Regarding this drug, Dr. William B. Bixler, an FDA veterinarian, wrote:

> This product [Adams No-Mo Tape Worm Expeller for Dogs] has been marketed since 1938 [sic; since 1925] and has been used successfully by many veterinarians with little or no adverse reactions at the dosages recommended.

8. That the standard pharmaceutical texts extant in 1962 recognized arecoline hydrobromide as generally safe and effective treatments for the claims made on the WRM-RID label. (See, "References Establishing that Arecoline Hydrobromide and Piperazine are Generally Recognized as Effective and Safe Treatments for Claims on WRM-RID Label," attached hereto as "Exhibit I."[1]

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[1]Rudolph Seider, Veterinary Drugs in Current Use; Animal Diseases U.S.D.A., 1956: Control of Tapeworms in Dogs and Cats: Arecoline hydrobromide used against common tapeworm affecting these animals only. Arecoline hydrobromide is a satisfactory treatment for removal of echinococcus, the hydatid tapeworm; Milk's Veterinary Pharmacology, Materia and Therapeutics, 6th Edition: Arecoline Hydrobromide Teniacide for Dogs and Cats: Generally considered a fairly reliable teniacide that works promptly and frequently gives very satisfactorily results. In experiments made on dogs it appeared that after previous treatment of small doses, the fatal dose apparently increased; Textbook of Organic Medicinal Pharmaceutical

9. That even as recently as 1988, the standard Pharmacology text used in Colleges of Veterinary Medicine throughout North America, i.e., Roberson, Edward L.: "Anticestodal and Antirematodal Drugs", Veterinary Pharmacology and Therapeutics, 6th ed, (See Exhibit "E"), stated the following regarding the safety and efficacy of arecoline hydrobromide:

> Indications: Arecoline hydrobromide (hereafter, arecoline) is effective against all tapeworms of dogs including Echinococcus. Laboratory-induced infections of Taenia piriformis, T. hydatigena, T. ovis, T.

Chemistry, 3rd. Edition; Dispensatory of the United States of America, 25th Edition, p. 1945; Merck Veterinary Manual, 2nd. Edition: In the treatment of tapeworm infections little attention is given to the type of cestode involved . . . arecoline hydrobromide (Rx 158) orally has been widely used in dogs. It is best given after a fast of twelve hours. In campaigns against hydatid disease arecoline hydrobromide has for several years been the drug of choice for the treatment of canine infection which echinococcus granuloses. Doses as high as 2 mg/lb body weight have been commonly employed ... the animals are not actually weighed since their tolerance for arecoline hydrobromide allows an estimation to suffice.; Merck Index, 7th Edition; Veterinary Drug Encyclopedia & Therapeutic Index, 9th Edition, pgs. 172, 248, 260; Bradley, R.E., Crinimins, Lt. T., Zweigart, T.F., J.A.V.M.A. 128 (1956) pgs. 393—394.

multiceps, and E. granuloses in dogs can be treated with a reasonable degree of success.

Until the advent of bunamidine (and subsequently praziquantel), arecoline was the only usable substance for treatment of Echinococcus in dogs. It is partially effective against nongravid and adult forms.

. . .

Toxicity. Emesis and exaggerated catharsis with liquid feces occur in a low percentage of dogs given a therapeutic dose of arecoline. These reactions are mild and only transitory without particular discomfort to dogs. The toxic effect of administering 44 mg/kg has been tested. Although dogs showed signs of extreme discomfort and convulsions, there were no deaths.

. . .

The drug is generally not used in cats because it is understood to cause excessive bronchial secretion which may cause suffocation. Brander and Pugh (1971) observed that no scientific corroboration substantiated this claim.

10 That the 1954 edition of J. Pharmacy and Pharmacology contains a report of a clinical study dealing with the safety and efficacy of piperazine as a veterinary anthelmintic. Drs. J. Sloan, P.A. Kingsbury, and D.W.

Jolly conclude that piperazine has "such a wide margin of safety that it will be of considerable value in veterinary therapeutics." Their conclusion is based on experimental results gathered in clinical studies performed pursuant to the generally accepted methods espoused by the scientific community at that time. (See: J.E.N. Sloan, P.A. Kingsbury, and D. Jolly in "Preliminary Trials with Piperazine Adipate as a Veterinary Anthelmintic," J. Pharmacy & Pharmacology, vol. VI, No. 10, October 1954, pps. 718-724. A copy of such article is attached hereto as Exhibit "F."[2]

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[2]It is interesting to note that the FDA has already admitted
in their answers to the following interrogatories **that the FDA has absolutely no evidence to support their accusation that WRM-RID is not safe**:

> Interrogatory Number 9:
> Please state if the plaintiff [FDA] has in its possession, or has knowledge of, any clinical data or tests regarding the use of, and the safety of WRM-RID.
> Response:
> ... **The plaintiff [FDA] does not have in its possession, nor does the plaintiff [FDA] have knowledge of, any adequate and well controlled clinical investigations conducted to establish the safety and efficacy of the combination product known as "WRM-RID" for use under the labeled**

11 That the safety and efficacy of arecoline hydrobromide has been established by evidence consisting of adequate and well-controlled investigations, including field investigations, by experts qualified by scientific training and experience. Drs. G.G. Gregory and J.D. McConnell clinically investigated the toxicity and efficiency of arecoline hydrobromide in the Tasmanian hydatid control program. Australian Veterinary Journal (1978) 54(4) 193-195 [En] Dep. Agric. P0 BOX 407, Launceston, Tasmania 7250, Australia, From Veterinary Bulletin 49, 448. (See Exhibit "H") The results of this clinical investigation revealed:

> Data on the efficiency and toxicity of arecoline hydrobromide during the first 11

> **indications.**
> Interrogatory Number 10:
> If you answer to interrogatory number 9 is "Yes," please state the name, title, address, and telephone number of each person in possession of such information.
> Response:
> ... **The plaintiff [FDA] does not have in its possession, or have any knowledge of, any clinical data or tests pertaining to toxicity from the use of WRM-RID in treating dogs and cats** that have been exposed to organophosphates.

A copy of the FDA'S complete answers to our interrogatories is attached hereto as "Exhibit G."

> years of the hydatid limitation program in Tasmania, Australia are presented. A satisfactory mucous purge was obtained from about 80% of dogs when arecoline was used at 3.25 mg/kg body-weight and from 75% when the dose rate was reduced to 1.62 mg.kg. . . . Toxicity was seen as acute cardiac collapse in about 5 dogs per 1000 dosed. Death followed in one dog in about 9500.

12 That WRM-RID formula is identical to the WRM-RID formula in existence on October 9, 1962; that WRM-RID was commercially available on October 9, 1962; that on October 9, 1962 WRM-RID and the active ingredients therein were generally recognized by experts as safe for their intended use; that WRM-RID is currently intended solely for use under the conditions prescribed or recommended on October 9, 1962; that WRM-RID was not within the definition of a "new drug" under the 1938 Federal Food, Drug and Cosmetic Act, and that WRM-RID was not, on October 9, 1962, covered by an effective New Drug Application under the 1938 Act.

Further Affiant sayeth naught.

/s/ William D. Semple
William D. Semple, President
Bingman Laboratories, Inc.

Sworn to before me and subscribed in my presence this 3rd day of November, 1995.

/s/ Carrie Ann Wilbur
NOTARY PUBLIC